Recommendations for the Use of Antiretroviral Drugs in Pregnant Women with HIV Infection and Interventions to Reduce Perinatal HIV Transmission in the United States

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Antepartum Care (Last updated January 17, 2020; last reviewed January 17, 2020)

General Principles Regarding Use of Antiretroviral Drugs during Pregnancy

Panel's Recommendations
• Initial evaluation of pregnant women living with HIV should include an assessment of HIV disease status and plans to initiate, continue, or modify antiretroviral therapy (ART) **(AI)**. The National Perinatal HIV Hotline (1-888-448-8765) provides free clinical consultation on all aspects of perinatal HIV care.
• All pregnant women with HIV should initiate ART as early in pregnancy as possible, regardless of their HIV RNA level or CD4 T lymphocyte count, for their own health and to prevent perinatal HIV transmission and secondary sexual transmission **(AI)**. The Panel on Treatment of Pregnant Women with HIV Infection and Prevention of Perinatal Transmission recommends that individuals with HIV maintain an HIV viral load that is below the limit of detection during pregnancy and postpartum and throughout their lives **(AII)**.
• To minimize the risk of perinatal transmission, antiretroviral (ARV) drugs should be administered at all time points (including antepartum and intrapartum) to the woman as well as postnatally to the neonate **(AI)**.
• The known benefits and potential risks of all medications, including ARV drugs used during pregnancy and postpartum, should be discussed with all women with HIV **(AIII)**.
• The importance of adherence to ARV drug regimens should be emphasized during patient counseling **(AII)**.
• ARV drug-resistance genotype evaluations or assays should be performed before starting ARV drug regimens in women who are ARV-naive **(AII)** or ARV-experienced **(AIII)** and before modifying ARV drug regimens **(AII)** in women whose HIV RNA levels are above the threshold for resistance testing (i.e., >500 copies/mL to 1,000 copies/mL).
• In pregnant women who are not already receiving ART, ART should be initiated before results of drug-resistance testing are available, because **earlier viral suppression has been associated with lower risk of transmission**. When ART is initiated before results are available, the regimen should be modified, if necessary, based on resistance assay results **(BIII)**.
• Coordination of services among prenatal care providers, primary care and HIV specialty care providers, and, when appropriate, mental health and substance use disorder treatment services, intimate partner violence support services, and public assistance programs is essential to help ensure that women with HIV adhere to their ARV drug regimens **(AII)**.
• Providers should initiate counseling about key intrapartum and postpartum considerations during pregnancy, including mode of delivery, lifelong HIV therapy, family planning and contraceptive options, infant feeding, infant ARV prophylaxis, and timing of infant diagnostic testing **(AIII)**.
Rating of Recommendations: *A = Strong; B = Moderate; C = Optional*
Rating of Evidence: *I = One or more randomized trials with clinical outcomes and/or validated laboratory endpoints; II = One or more well-designed, nonrandomized trials or observational cohort studies with long-term clinical outcomes; III = Expert opinion*

In addition to the standard antenatal assessments for all pregnant women, the initial evaluation of women living with HIV should include an assessment of HIV disease status and recommendations for HIV-related medical care. This initial assessment should include the following:

- Review of prior HIV-related illnesses and past CD4 T lymphocyte (CD4) cell counts and plasma HIV RNA levels;
- Current CD4 count;
- Current plasma HIV RNA level;
- Assessment of the need for prophylaxis against opportunistic infections, such as *Pneumocystis jirovecii* pneumonia (see the Adult and Adolescent Opportunistic Infections Guidelines);
- Screening for hepatitis A virus (HAV), hepatitis C virus, and tuberculosis in addition to standard screening for hepatitis B virus (HBV);

- Screening for and treatment of sexually transmitted infections (STIs), such as syphilis, *Chlamydia trachomatis*, *Trichomonas vaginalis*, and *Neisseria gonorrhea*;[1-3]
- Assessment of the need for HAV, HBV, influenza, pneumococcus, and Tdap immunizations;[4,5]
- Complete blood cell count and renal and liver function testing;
- HLA-B*5701 testing if the use of abacavir is anticipated (see Table 8);
- History of prior and current antiretroviral (ARV) drug use, including prior ARV drug use for the prevention of perinatal transmission or treatment of HIV;
- History of adherence problems;
- Results of prior and current ARV drug-resistance tests;
- History of adverse effects or toxicities caused by previous ARV regimens;
- Screening for depression and anxiety and an assessment of the need for supportive care (e.g., mental health services, substance use disorder treatment services, smoking cessation), as well as support to help ensure lifelong adherence to antiretroviral therapy (ART);[6]
- Screening for intimate partner violence and assessment of the need for interventions or referrals for supportive care;
- Referral of sexual partner(s) for HIV testing and ARV treatment or prophylaxis; *and*
- Referral of children for HIV testing.

The National Perinatal HIV Hotline

The National Perinatal HIV Hotline (1-888-448-8765) is a federally funded service that provides free clinical consultation to providers who are caring for women with HIV and their infants.

How Antiretroviral Drugs Prevent Perinatal Transmission and Improve Maternal Health

All pregnant women with HIV should receive ART early in pregnancy, regardless of their viral load or CD4 count, for their own health and for the prevention of perinatal HIV transmission and secondary sexual transmission. ARV drugs are important for maintaining maternal health because they decrease the rate of HIV disease progression, reduce the risk of opportunistic disease, and reduce the risk of maternal death.

ARV drugs reduce the risk of perinatal transmission of HIV in all pregnant women, regardless of their CD4 counts and HIV RNA levels. ARV drugs can reduce the risk of perinatal transmission through several mechanisms. Antenatal drug administration decreases maternal viral load in blood and genital secretions.[7-9] Strict adherence to an ARV regimen is needed to achieve rapid viral suppression and minimize the risk of perinatal transmission. Although the risk of perinatal transmission in women with undetectable plasma HIV RNA levels appears to be extremely low, perinatal transmission has been reported among women on ART (see Recommendations for Use of Antiretroviral Drugs During Pregnancy).[10-13] Studies have reported low-level cervicovaginal HIV RNA and DNA shedding in women who were on ART and who had undetectable plasma viral loads.[14-16] Penetration of ARV drugs into the female genital tract varies by drug.[17-20]

Infant pre-exposure prophylaxis should also be used to prevent perinatal transmission, as maternal viremia is not the only risk factor for HIV transmission. Pre-exposure prophylaxis is achieved by administering ARV drugs to the mother that cross the placenta and produce adequate systemic drug levels in the fetus. In addition, infant post-exposure prophylaxis is achieved by administering ARV drugs to the infant after birth, providing protection from cell-free or cell-associated virus that may have entered the fetal/infant systemic circulation during labor and delivery. The importance of the pre- and post-exposure components

of prophylaxis in reducing the risk of perinatal transmission is demonstrated by the reduced efficacy of interventions that involve administration of ARV drugs only during labor and/or to the newborns.[21-28] Therefore, using a combination of preconception ART, confirmation of antepartum plasma viral load suppression, scheduled surgical delivery (if indicated based on most recent maternal plasma viral load), intrapartum continuation of the current regimen with the addition of intravenous zidovudine (if indicated, based on the most recent maternal plasma viral load), and infant ARV prophylaxis is recommended to prevent perinatal transmission of HIV.

General Principles of Drug Selection

In general, the recommendations for the use of ART in pregnant women are the same as those for women who are not pregnant. However, the Perinatal Guidelines may differ from the Adult and Adolescent Antiretroviral Guidelines in some instances where regimen selection has been modified based on concerns about specific drugs or limited experience with newer drugs during pregnancy (see Table 4 and Recommendations for Use of Antiretroviral Drugs During Pregnancy).

Clinicians and patients should discuss the substantial benefits of ARV drugs for maternal health and for reducing the risk of transmission of HIV to infants; this helps put the potential risks of using these drugs into perspective (see Table 8 and Appendix B: Supplement: Safety and Toxicity of Individual Antiretroviral Agents in Pregnancy). Counseling of pregnant women about ARV drug use should be directive and noncoercive, and providers should help women make informed decisions regarding the use of ARV drugs.

Discussions with women about initiation of ART regimens should include information about:

- Maternal risk of disease progression and the benefits and risks of therapy for maternal health;[29]
- The benefits of ART for preventing perinatal transmission of HIV;[11]
- The benefits of using ART to achieve and maintain viral suppression, which reduces the risk of sexual transmission to partners who do not have HIV;[30]
- The need for strict adherence to the prescribed drug regimen to avoid resistance, optimize health outcomes, and minimize the risk of perinatal HIV transmission;
- The potential adverse effects of ARV drugs for women, fetuses, and infants, including potential interactions with other medications the women may already be receiving (see Recommendations for Use of Antiretroviral Drugs During Pregnancy);[31-33] *and*
- The limited long-term outcome data for infants who were exposed to ARV drugs in utero, especially for newer ARV drugs.

In pregnant women with HIV who are not currently receiving treatment, plasma HIV RNA levels should be measured and ART should be initiated. In women with plasma HIV RNA levels above the threshold for standard genotypic resistance testing (i.e., >500 copies/mL to 1,000 copies/mL), ARV drug-resistance testing should be sent off before starting ART; however, ART should be initiated before results of drug-resistance testing are available, because earlier viral suppression is associated with a lower risk of perinatal transmission.[34,35] The ART regimen can be modified, if necessary, based on resistance assay results[36] (see Antiretroviral Drug Resistance and Resistance Testing in Pregnancy). Counseling should emphasize the importance of adherence to the ARV drug regimen to minimize the development of resistance and support the effectiveness of ART in achieving viral suppression. Women with poor adherence during pregnancy are more likely to have detectable viral loads at delivery.[37]

Transplacental passage of ARV drugs is thought to be an important mechanism of infant pre-exposure prophylaxis. Thus, when selecting an ARV regimen for a pregnant woman, at least one nucleoside reverse transcriptase inhibitor agent with high placental transfer should be included as a component of the ART regimen (see Table 8).[38-42]

Patient Counseling and Coordination of Care

Coordination of services among prenatal care providers, primary care and HIV specialty care providers, mental health and substance use disorder treatment services, and public assistance programs is essential to ensure that women with HIV are well supported during all stages of their pregnancies and during the postpartum period. Medical care of pregnant women with HIV requires coordination and communication between HIV specialists and obstetric providers. General counseling should include current knowledge about risk factors for perinatal HIV transmission. Risk of perinatal transmission of HIV has been associated with potentially modifiable factors, including cigarette smoking, substance use disorders, and genital tract infections. Besides improving maternal health, cessation of cigarette smoking and drug use and treatment of STIs and other genital tract infections may reduce the risk of perinatal transmission. Women should be screened for mental health conditions, assessed for the risk of intimate partner violence, counseled about disclosure of their HIV status when needed, and referred to the appropriate services.

In addition, providers should counsel women with HIV about what to expect during labor, delivery, and the postnatal period. This includes discussing the mode of delivery and the possible use of intrapartum zidovudine, as well as family planning and contraceptive options during the postpartum period. Providers should also discuss the possibility of simplifying a woman's ARV regimen after delivery, which can help promote long-term adherence to ART. Discussions regarding the prevention of postnatal transmission to the neonate should also include recommendations about infant feeding, neonatal ARV prophylaxis, infant diagnostic HIV testing, and the avoidance of premastication of food (see Counseling and Managing Women Living with HIV in the United States Who Desire to Breastfeed).

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